Remarks/Arguments

Applicants respectfully request that the Examiner reconsider the application in light of the foregoing amendments and remarks presented below.

Rejection under 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 1, 3, 5, 7, 18, 20 and 22-24 under 35 U.S.C. §112, first paragraph, because the specification does not reasonably provide enablement for performing the methods recited in claims 1, 3, 5, 7, 18, 20 and 22-24 when a complex biological construct does not contain genetic materials (DNA and/or RNA).

As defined in the specification at page 9 in paragraphs 23 and 24, a complex biological construct is an entire limb of animal or other gross anatomical structure such as appendages, organs, collection of organs, or organ systems. The complex biological construct may also be hair, bone, blood, blood vessels, muscles, connective tissue, cartilage, nerve, bone marrow, epithelium, and adipose tissues" and may contain many of the tissues that make up animal.

The complex biological construct of the present invention contains genetic molecules. For example, at pages 18 and 19, the specification describes when the complex biological construct is liquefied, cell lysis occurs, and the cell's plasma membrane is ruptured together with its contents including all of the chromosomal DNA and RNA. As a matter of clarity, therefore, the claims have been amended in order that the complex biological construct comprises genetic molecules to remove what the Examiner has described as the "unpredictable factor" at page 4 of the office action.

Rejection under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 1-7 and 18-24 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 18 have been amended to include the words "a solution" in the liquefying step.

Claims 1 and 18 have been amended to "a method of analyzing expression of a gene" and "determining expression of said gene." It should now be clear that the kind of gene expression to be determined is that of the specific gene(s) being analyzed.

Claims 3 and 20, among others, have been amended to include that the complex biological construct of the present invention contain genetic molecules. There should now be sufficient antecedent basis for the limitation of "isolating genetic molecules."

Claim 3 has been amended to add the step of "determining expression of said gene." Therefore the goal "of analyzing expression of a gene" in the preamble can be reached.

Claims 4 and 21 have been amended to refer to "wherein said component ruptures cells present within said complex biological construct." Antecedent basis should no longer be required.

Claim 6 has been amended to depend form claim 5 where there is sufficient antecedent basis for "said gene expression analysis."

Claim 23 has been amended to depend form claim 22 where there is sufficient antecedent basis for "said gene expression analysis."

Applicant respectfully requests that the Examiner reconsider the rejection of claims 1-7 and 18-24 under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102(e)

The Examiner has rejected claims 1 and 18 under 35 U.S.C. §102(e) as being anticipated by Lockhart *et al.* However, Lockhart *et al* does not anticipate the claims of the subject application.

First, as recognized by the Examiner, Lockhart *et al.* does not disclose a complex biological construct or a gross anatomical structure of an animal comprising more than one type of tissue. As described in paragraph 23 of the specification of the present application, a "complex biological construct" is "any portion of an animal having more than one tissue type. The complex biological construct may comprise an entire limb of animal or other gross anatomical structure such as appendages, organs, collection of organs, or organ systems. The complex biological construct may include hair, bone, blood, blood vessels, muscles, connective tissue, cartilage, nerve, bone marrow, epithelium, and adipose tissues."

Second, Lockhart *et al* does not teach a method of liquefying a complex biological construct comprising more than one tissue type in order that the cytoplasm of the cell be broken and the cell contents released. Third, Locket *et al* does not teach a method of analyzing gene expression by first liquefying different tissue, particularly tissue from a single anatomical structure.

Indeed, Lockhart *et al* teaches away from the subject invention. At Columns 11 beginning line 33 through Column 12, line 55, Lockhart et al teaches that the sample is a homogenate of cells or tissues or other biological samples, and that "preferably such sample is a total RNA preparation of a biological sample." Col. 11, ls. 33 through 62. .Furthermore, the examples taught by Lockhart are single human tumor cell lines, not multiple cell lines. Lockhart *et al* does not anticipate the claims of the subject application.

Rejection under 35 U.S.C. §102(b)

The Examiner has rejected claims 3, 4, 20 and 21 under 35 U.S.C. §102(b) as being anticipated by Sambrook *et al.* Sambrook *et al.* does not disclose the use of a complex biological construct. As discussed above, a "complex biological construct" of the subject invention is any portion of an animal having more than one tissue type. The complex biological construct may comprise an entire limb of animal or other gross anatomical structure such as appendages, organs, collection of organs, or organ systems. The complex biological construct may include, but are not limited to, hair, bone, blood, blood vessels, muscles, connective tissue, cartilage, nerve, bone marrow, epithelium, and adipose tissues.

The teaching of Sambrook *et al.*, however, is directed to isolating RNA from cells that cannot be fractionated easily into cytoplasm and nuclei (frozen fragment of tissue). *See* page 7.18, first paragraph, of Sambrook *et al.* Sambrook *et al* does not teach or describe a step of liquefying a complex biological construct and transferring the solution to a microarray for analysis. But rather, Sambrook *et al* teaches multiple steps of centrifugation and washing and once frozen adding a buffer while the powdered cell is still frozen. Moreover, Sambrook *et al* teaches away from the present invention because chaotropic agents are recommended by Sambrook *et al* to increase yield and quality of RNA. For reasons provided above, claims 3, 4, 20 and 21 of the present application are not anticipated by Sambrook *et al.*

Rejection under 35 U.S.C. §102(e)

The Examiner has rejected claims 3-7 and 20-24 under 35 U.S.C. §102(e) as being anticipated by Lockhart *et al.* as evidenced by Sambrook *et al.* A 35 U.S.C. §102(e) rejection based on Lockhart et al. as evidenced by Sambrook *et al.* is improper. The court in *In re Saunders,* 444 F.2d 599, 602-03, 170 USPQ 213 (CCPA 1971) found that only one reference can be used to show the elements of the claimed invention. MPEP 2131.01 states that an extra reference can be used to show that the reference provides an enabled disclosure, explain the meaning of a term or to show that a characteristic not disclosed in the reference is inherent. The court in *In re Baxter Travenol Labs,* 952 F.2d 388, 390 (Fed. Cir. 1991) found that the extra reference can be used to explain but not expand the meaning of the reference. Sambrook *et al.* is used to expand the teaching of Lockhart *et al.* because missing from Lockhart's disclosure are the steps of removing and purifying/extracting/isolating the genetic molecules. But, even with the additional disclosure from Sambrook, Lockhart does not anticipate the claims of the subject invention because Lockhart does not disclose a liquefied complex biological construct.

Therefore, this rejection is improper because Lockhart does not anticipate the present invention, and to interpret Lockhart *et al,* an allegedly anticipating reference, by incorporating the specific teachings of a second reference (Sambrook et al) is impermissible. Lockhart *et al* fails to teach liquefying a complex biological construct as defined in the specification of the subject application to prepare a gene expression analysis and Sambrook et al cannot be used to expand the teaching of Lockhart *et al.* to include purification steps not taught.

Rejection under 35 U.S.C. §103(a)

The Examiner has rejected claims 2 and 19 under 35 U.S.C. §103(a) as being unpatentable over Lockhart *et al.* as applied to claims 1 and 18 above, and further in view of Pittman *et al.* As discussed above, Lockhart *et al.* does not disclose liquefying a complex biological construct. Like Lockhart *et al.*, Pittman *et al.* does not teach liquefying a complex biological construct. Moreover, while Pitman *et al* teach isolation of RNA from mouse paw, Pitman *et al* teach using frozen tissue, grinding it into a powder and adding liquid nitrogen. See Example 2. Pitman does not teach liquefying the paw containing the genetic molecules and analyzing the expression of one or more genes.

Furthermore, there is no motivation for one skilled in the art to combine the teachings of Pitman *et al* with the teaching of Lockhart *et al* and arrive at the invention of the subject invention as presently claimed. The prior art must suggest the modification, and no suggestion is taught by either reference. Even though the teachings of Lockhart *et al* and Pitman *et al* may appear modifiable in manner the will yield the invention, it is only through hindsight motivation would these references be combined to teach the present invention.

Moreover, Pittman *et al.* teaches away from liquefying a complex biological construct to analyze gene expression. In paragraphs [0090] and [0091], Pittman *et al.* states "When obtaining the cells, it is preferable to obtain a sample continuing predominantly cells of the desired type, e.g., a sampled of cells in which at least about 50%, preferably at least about 60%, even more preferably at least about 70%, 80% and even more preferably, at least 90% of the cells are of the desired type. A higher percentage of cells of the desired type is preferable, since such a sample is more likely to provide clear gene expression data. It is also possible to obtain a

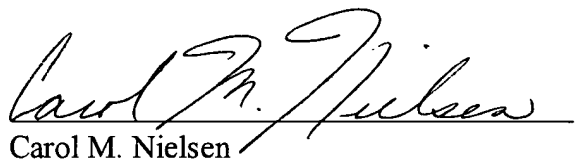
cell sample from a subject, and then to enrich it for a desired cell type . . . . Where the desired cells are in a solid tissue, particular cells can be dissected out, e.g., by microdissection."

Both Pitman *et al* and Lockhart *et al* teach the failure by others to yield sufficient amount of RNA from a sample unless that sample is first sufficiently purified and separated. However, applicants have resolved this long felt need by unexpectedly liquefying a complex biological construct to provide a sufficient amount of RNA for the gene expression analysis.

In light of the foregoing amendments and remarks, Applicants respectfully request that the rejections of the claims under 35 U.S.C. § 112 first and second paragraphs, 35 U.S.C. § 102 (b) and (e), and 35 U.S.C. § 103 be withdrawn, the application be allowed and pass to issuance.

Respectfully submitted,

Date: April 11, 2005

By: 
Carol M. Nielsen
Reg. No. 37,676

Winstead Sechrest & Minick P.C.
2400 Bank One Center
910 Travis Street
Houston, TX 77002
713-650-2722 phone
713-650-2400 fax
cnielsen@winstead.com

Attorney Docket No. 43407-P002US